PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

Roche Diagnostics GmbH
Patent Department Penzberg
ABK | BK | 04 Juli 2005 | WN | WJ | BUR | HH | HIL | MI | WRI

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Applicant's or agent's file reference see form PCT/ISA/220 22394 WO-WJ	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2005/003345	31.03.2005	01.04.2004

International Patent Classification (IPC) or both national classification and IPC
A61K31/515, A61K31/724, A61P11/00

Termin
01.10.2005 not.
(20.08.05)

Applicant
F. HOFFMANN-LA ROCHE AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

Termin
01.02.2006 not.
(20.12.05)

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2005/003345

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 4,6

because:

☒ the said international application, or the said claims Nos. 4,6 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. -

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2005/003345

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-6
	No:	Claims	
Inventive step (IS)	Yes:	Claims	2-6
	No:	Claims	1
Industrial applicability (IA)	Yes:	Claims	1-3,5
	No:	Claims	

2. Citations and explanations

see separate sheet

SECTION III

Claims 4,6 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

SECTION V

1. The following documents are referred to in this communication; the numbering will be adhered to in the rest of the procedure. If not otherwise specified, reference is made to the corresponding passages cited in the search report.

   D1: WO 98/58925 A
   D2: WO 02/34753 A
   D3: WO 02/34726 A

   D1 deals with barbituric acid derivatives which can be used in the treatment of various diseases including tumour, inflammation and emphysema. Table I shows the IC_{50} of some compounds in relation to MMP-9, said IC_{50} results to be 19.5 nM and 20 nM, respectively for the two tested compounds.
   D2 and D3 deal with derivatives of trioxopyrimidine which act as MMP-inhibitors. They may be used for the treatment of various diseases including chronic obstructive pulmonary disease, asthma, emphysema.

2. The present application meets the requirements of Article 33(1) PCT, because the subject-matter of claims 1-6 appears to be new in the sense of Article 33(2) PCT.

3. The present application does not meet the requirements of Article 33(1) PCT, because the subject-matter of claim 1 does not involve an inventive step in the sense of Article 33(3) PCT.
   The problem to be solved by the present application may be regarded as how to provide a new medical use for trioxopyrimidine compounds with MMP inhibitory activity. The

solution proposed by the present application is to provide compounds which possess a specific IC_{50} toward MMP-1, MMP-2, MMP-3, MMP-9, MMP-14.
D1 describes compounds which display this specific IC_{50} with regards to MMP-9. In D1 IC_{50} of said compounds has not be measured for the remaining MMP, hence the possibility exists that said compounds would fulfil the functional definition of claim 1 of the present application. Moreover, poor explanation is given in the application on the reason/motivation why the IC_{50} values have to fulfil the requirements if claim 1 and on the advantage achieved through said feature.

4. For the assessment of the present claims 4,6 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.